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and NFAT4 genes in the genome of said embryonic stem cell to produce a transgenic embryonic stem cell; and

c) introducing said transgenic embryonic stem cells into said pseudopregnant mouse under conditions such that said pseudopregnant mouse produces progeny comprising a functionally disrupted NFATp gene and a functionally disrupted NFAT4 gene.

Amend
50. (New) A murine cell comprising a disrupted NFATp gene and a disrupted NFAT4 gene.

51. (New) The murine cell of claim 50, wherein said cell is selected from the group consisting of fertilized egg cells, embryonic stem cells and lymphoid cells.

REMARKS

Claims 1-31 were present in the application as filed. Claims 2-31 have been canceled herein without prejudice. Claims 32-51 have been added. Accordingly, claims 1 and 32-51 are currently pending in the application. For the Examiner's convenience, a copy of the currently pending claims are attached hereto as Appendix A.

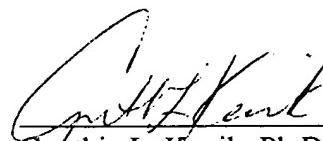
No new matter has been added. Support for the newly added claims can be found throughout the specification and in the claims as originally filed. Specifically, support for the newly added claims can be found, for example, at pages 36-41, in Examples 1-3, of the instant specification.

BEST AVAILABLE COPY Cancellation of and/or amendment to the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to expedite prosecution of the above-identified application. Applicants reserve the right to further prosecute the same or similar claims in the instant or in another patent application(s).

CONCLUSION

Applicants respectfully submit that the application is now in condition for allowance. If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' Attorney at (617) 227-7400.

Respectfully submitted,



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APPENDIX A

1. A method of identifying a compound that modulates an immune response comprising:
- a) contacting immune cells deficient in NFATp and NFAT4 with a test compound; and
 - b) determining the effect of the test compound on the activation of immune cells, the test compound being identified as a modulator of an immune response based on the ability of the test compound to modulate the activation of immune cells deficient in NFATp and NFAT4.
32. (New) A transgenic mouse comprising in its genome a first exogenous nucleic acid molecule that functionally disrupts a NFATp gene of said mouse and a second exogenous nucleic acid molecule that functionally disrupts a NFAT4 gene of said mouse.
33. (New) The transgenic mouse of claim 32, wherein the phenotype of said mouse is characterized by lymphadenopathy relative to a wild-type mouse
34. (New) The transgenic mouse of claim 32, wherein the phenotype of said mouse is characterized by splenomegaly relative to a wild-type mouse.
35. (New) The transgenic mouse of claim 32, wherein the phenotype of said mouse is characterized by blepharitis relative to a wild-type mouse.
36. (New) The transgenic mouse of claim 32, wherein the phenotype of said mouse is characterized by interstitial pneumonitis relative to a wild-type mouse.
37. (New) The transgenic mouse of claim 32, wherein said mouse displays an increase in peripheral T cells relative to a wild-type mouse.
38. (New) The transgenic mouse of claim 37, wherein said peripheral T cells have a memory/activated phenotype relative to a wild-type mouse.
39. (New) The transgenic mouse of claim 32, wherein said mouse displays compromised FasL expression relative to a wild-type mouse.
40. (New) The transgenic mouse of claim 39, wherein said mouse displays defective apoptosis relative to a wild-type mouse.

41. (New) The transgenic mouse of claim 32, wherein said mouse displays increased Th2 cytokine production relative to a wild-type mouse.

42. (New) The transgenic mouse of claim 41, wherein said Th2 cytokine is IL-4.

43. (New) The transgenic mouse of claim 42, wherein said mouse displays increased expression of IL-4 dependent immunoglobulin isotypes.

44. (New) The transgenic mouse of claim 43, wherein said immunoglobulin isotypes are IgG1 and IgE.

45. (New) A method for identifying a test compound that regulates Th2 cell activity comprising:

a) providing:

i) first and second transgenic mice comprising a genome deficient in NFATp and NFAT4; and

ii) a composition comprising said test compound; and

b) administering said test compound to said first transgenic mouse; and

c) evaluating Th2 cell activity in said first transgenic mouse relative to Th2 cell activity in said second transgenic mouse to thereby identify a compound that regulates Th2 cell activity.

46. (New) The method of claim 45, wherein said test compound is at least one peptidic compound derived from the calcineurin-interacting region of NFATp or NFAT4.

47. (New) The method of claim 45, wherein said test compound comprises the amino acid sequence of SEQ ID NO: 1.

48. (New) The method of claim 45, wherein said peptidic compound comprises the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 3.

49. (New) A method for producing a transgenic mouse, wherein said mouse exhibits a phenotype characterized by increased Th2 cytokine production relative to a corresponding wild-type mouse, comprising:

a) providing (1) an embryonic stem cell comprising wild-type NFATp and NFAT4 genes; (2) a pseudopregnant mouse; and (3) an exogenous nucleic acid molecules comprising at least a portion of NFATp and a NFAT4 gene, said portion comprising one or more deletions in one or

more exons of said NFATp and NFAT4 genes;

b) introducing said nucleic acid molecules into said embryonic stem cell under conditions such that said nucleic acid molecule functionally disrupts at least one of said wild-type NFATp and NFAT4 genes in the genome of said embryonic stem cell to produce a transgenic embryonic stem cell; and

c) introducing said transgenic embryonic stem cells into said pseudopregnant mouse under conditions such that said pseudopregnant mouse produces progeny comprising a functionally disrupted NFATp gene and a functionally disrupted NFAT4 gene.

50. **(New)** A murine cell comprising a disrupted NFATp gene and a disrupted NFAT4 gene.

51. **(New)** The murine cell of claim 50, wherein said cell is selected from the group consisting of fertilized egg cells, embryonic stem cells and lymphoid cells.

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